

13. Mch. 1436

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❖ Renal system ❖

Introduction to renal physiology

Physiology

Lecture (1)

① The renal system consist of the :-

- I. Kidneys.
- II. Ureters.
- III. Urinary bladder.
- IV. Urethra.

② Functions of the Kidney :-

- I. Excretion of waste products.
- II. Regulates E.C.F electrolytes. (Concentration = maintain osmolality).
- III. Regulates E.C.F Volume.
- IV. Regulates E.C.F pH.
- V. Regulates the blood pressure.
- VI. Endocrine functions :
 - Erythropoietin.
 - prostaglandin.
 - Activation Vitamin D

The kidney is an important organ in homeostasis.

③ Functional anatomy of the Kidney :-

- ✓ Kidney is a bean shaped, retroperitoneal organ it surrounded by a capsule which is thin but tough.
- ✓ The medial end of the kidney has a hilum through which passes the renal artery, renal vein, Ureter, renal nerve and lymphatics.

- ✓ Urea will be collected in minor calyces → Which unite to form major calyces → Unite to form the renal pelvis then → Urine passes across the ureters to the urinary bladder.

⑥ Renal blood supply:-

- ✓ Renal artery is a direct branch from the aorta.
 - ✓ It gives short & straight branches
- main {
- 1. Renal artery
 - 2. Interlobar arteries
 - 3. Arcuate arteries.
 - 4. Interlobular arteries.
 - 5. Afferent arteriole.
 - 6. Glomerular capillaries.
 - 7. Efferent arteriole
 - 8. Peritubular capillaries.
 - 9. Small veins.
 - 10. Renal veins.
- Branches {

➤ In a longitudinal section the kidney is made of two areas:

- Cortex (outer layer).
- Medulla (inner layer formed of pyramids).

- ❖ The functional unit of the kidney is the nephron.
- ❖ There is about one million nephron in each kidney.
- ❖ The nephron is made of two parts:

(1) Glomerulus.

(2) Renal tubule.

✓ The glomerulus: →

➤ Structure of glomerulus: -

• Formed by:

i. Glomerular capillaries: Applied by the afferent and drained by slightly smaller efferent arteriole (not vein).

ii. Bowman's capsule: Surrounded the capillary bed.

➤ Function of glomerulus: -

The main function of glomerulus is

Filtration.

- Mesangial cells are present between the glomerular capillaries.
- They are contractile and phagocytic.

✓ The renal tubule: →

I. proximal convoluted tubule.

II. Loop of henle.

III. Distal convoluted tubule.

IV. Collecting duct.

I. Proximal convoluted tubule (P.C.T) :

- Luminal brush border (to increase the surface area for reabsorption).
- A lot of mitochondria (very active cell).

II. Loop of henle :

➤ (3) parts:

- a) Thin descending
- b) Thin ascending
- c) Thick ascending

➤ There are (2) types of nephrons :-

(1) Cortical nephron:

- ✓ 85% of nephron.
- ✓ Their glomeruli high up in the cortex.
- ✓ Their loop is short which has no thin ascending part.

(2) Juxta medullary nephron:

- ✓ 15% of nephron.
- ✓ Their glomeruli lie deep in the cortex.
- ✓ They have long loops with thin ascending part.
- ✓ They are very important for concentration of urine.

◎ Renal blood flow (RBF) :-

- ✓ Is 25% of cardiac output (1042 - 1.5 L/min)
- ✓ 90% of this blood perfuse the cortex.
- ✓ Only 10% perfuse the medulla.

➤ Regulation of RBF :

(1) Auto regulation

(2) Neural regulation

(3) Hormonal regulation.

- The kidney is able to maintain its blood flow inspite of changes in blood pressure.
- This can be done by changing the radius of the arterioles specially the afferent arteriole.
- The RBF remain relatively constant when the perfusion pressure ^{is} between 80-180 mmHg.
- if the pressure drops < 60 mmHg drops steeply and acute renal failure may occur.

(1) Auto-regulation :

Is due to :

- [i] Myogenic response : Smooth muscle of renal arterioles contract in response to stretch
- [ii] Tubuloglomerular feedback : Macula densa detects changes in perfusion pressure

by detecting changes in the tubular flow and causes secretion of a vasoactive substance.

(2) Neural-regulation:

- Renal sympathetic nerve stimulation causes constriction of both afferent & efferent arteriole $\rightarrow \downarrow$ RBF.

- The afferent arteriole is more sensitive than efferent arteriole.

(3) Hormonal-regulation:

- Angiotensin constrict both afferent and efferent arteriole.

- The efferent is more sensitive.

- Epinephrine and norepinephrine cause vasoconstriction, The afferent is more sensitive.

Glomerular Filtration③-renal processes result in urina formation:

- (i) **Filtration:** Function of the glomerulus.
- (ii) **Reabsorption:** of substance from the renal tubules into the body.
- (iii) **Secretion:** of substance from the blood into the renal tubules.

(i) Glomerular Filtration (GF) -

- ✓ Is a filtration across the glomerular capillaries.
- ✓ GF is defined as: The passage of fluids and crystalloid from the glomerular capillaries to the Bowman's space.
- ✓ It is a passive process (does not need energy).
- ✓ The filtration membrane is composed of:
 - a. Endothelial cells of the glomerular capillaries which are fenestrated (have pores) $\parallel 70-90 \text{ nm} \parallel$ in diameter.
 - b. Basement membrane.
 - c. Epithelium of the Bowman's capsule from podocytes that interdigitate to form filtration slits $\approx (25 \text{ nm})$ wide.

➤ Filtration pressure:

- The renal arterioles are short straight branches arising at the right angle from the renal artery.
- The afferent arteriole has the same pressure as the aorta (100 mmHg).
- Therefore the glomerular capillary pressure is high (45-60 mmHg).
- The systemic capillary pressure is $\approx (15-35 \text{ mmHg})$

➤ Net filtration pressure:

- (It is determined by the starling forces.)
- Hydrostatic pressure in glomerular capillary = 45 mmHg.
- Hydrostatic pressure in Bowman's space = -10 mmHg.
- Oncotic pressure in glomerular capillary = -25 mmHg.

- Oncotic pressure in Bowman's capsule nearly zero
- The Net filtration pressure $\longrightarrow = +10$ mmHg.
- ✓ The normal range of filtration pressure (10-15) mmHg
- ✓ Net filtration pressure always favors movement of fluid out of the glomerular capillary (Filtration).

➤ Composition of the filtrate:

- It is an ultra filtrate in plasma.
- Similar to plasma except that it doesn't contain plasma protein.
(GFR = Plasma - plasma proteins).

➤ Glomerular Filtration Rate:

- The normal glomerular rate is 125 ml/min.
- GFR in females < males by 10%.
- $GFR = 125 \text{ ml/min} = 7.5 \text{ L/hour} = 180 \text{ L/day}$.
- ✓ Therefore the volume of plasma is 3L.
- ✓ The plasma is filtrated about 60 times / day.
- ✓ $GFR = 180 \text{ L/day}$.
- ✓ Urine output is 1-1.5 L/day.
- ✓ Most of the fluid is reabsorbed in the renal tubules.

➤ Filtration Fraction:

- The ratio of the GFR to the renal plasma flow (RPF) is known as: The filtration fraction.
- Filtration fraction = $GFR / RPF = 125 / 605 \text{ ml/day} = 20\%$
- 20% of all freely filtrated substances.
(e.g: 20% of Na^+ that enters the kidney are filtrated into Bowman's space).
- Filtration fraction normally (0.16 - 0.20).

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Glomerular Filtration Rate

Control of GFR: →

GFR Can be expressed by Starling equation

$$GFR = K_f [(P_a - P_b) - (\pi_a - \pi_b)]$$

$K_f \equiv$ GF Coefficient (S.A permeability).

$P \equiv$ Hydrostatic pressure.

$\pi \equiv$ Oncotic pressure.

$G \equiv$ glomeruli.

$B \equiv$ Bowman's space.

► GFR is controlled by following factors:

(1) Surface area:

Is a size of the capillary bed along which filtration occurs.

✓ It is about 0.8 m^2 .

✓ Surface area can be changed by contraction and relaxation of the mesangial cells present between the glomerular capillaries.

E.g:

- Angiotensin II Cause contraction of the mesangial cells → ↓ S.A → ↓ GFR.

- ANP and dopamine Cause relaxation of mesangial cells.

(2) Permeability:

permeability of the glomerular capillary is 50 times that of muscle capillary.

✓ Permeability of a substance depend on:

(a) **Size**: neutral substance $> 8 \text{ nm}$ in diameter are not filtered, neutral substances with diameter $< 4 \text{ nm}$ are freely filtered, $4-8 \text{ nm}$ filtration is inversely proportionate to diameter.

(b) **Shape**: regular shape filtered easier.

(c) **Charge**: filtration of anionic substances $< 6 \text{ nm}$ in diameter is less than half that of the neutral substances of same size.

(3) **Hydrostatic pressure gradient**:

✓ Hydrostatic pressure gradient between the glomerular capillary & Bowman's space.

✓ Glomerular capillary pressure is higher than the other systemic capillary pressure because:

i. It is drained by arteriole.

ii. The renal arterioles are short & straight branches this will not waste the pressure.

(4) **Oncotic pressure gradient**:

✓ In the glomerular capillaries the oncotic pressure is 25 mmHg . (like the systemic capillaries).

✓ It tends to keep fluid in the glomerular capillaries.

✓ Oncotic pressure in Bowman's space is normally zero.

✓ Oncotic pressure in glomerular capillaries increases as fluid filtered.

✓ Oncotic pressure in the efferent arteriole is $>$ oncotic pressure in the afferent arteriole.

➤ Factors affecting the GFR:

(1) Change in the renal blood flow $\text{RBF} \rightarrow \text{GFR}$.

(2) Change in the glomerular capillary hydrostatic p. could be due to:

I. Change in the systemic BP:

✓ The kidney auto regulated its blood flow at range of $80 - 180 \text{ mmHg}$.

✓ Decrease in arterial pressure $< 80 \text{ mmHg}$ will cause a sharp drop in RBF & in GFR.

✓ Acute renal failure may follow hemorrhage.

✓ Urine volume has to be monitored after hemorrhage.

II. Afferent & Efferent arteriolar constriction:

✓ Afferent arteriolar constriction $\rightarrow$ $\downarrow$ filtration pressure $\rightarrow$ $\downarrow$ GFR
(e.g. Sympathetic stimulation).

✓ Efferent arteriolar constriction $\rightarrow$ $\uparrow$ filtration pressure $\rightarrow$ $\uparrow$ GFR.

✓ if constriction is severe & continued for long time $\rightarrow$ $\downarrow$ RBF $\rightarrow$ $\downarrow$ GFR.

(3) Change in Bowman's space hydrostatic pressure:

⊗ $\uparrow$ H.P in Bowman's space $\rightarrow$ $\downarrow$ GFR

[e.g. 1. (Uretric obstruction): Stone, tumor, fibrosis (schistosomiasis)

2. edema of the kidney: tight renal capsule limit]
swelling $\rightarrow$ increase tissue H.P.

e.g.: inflammation, toxicity.

(4) Change capillary oncotic pressure:

⊗ $\uparrow$ O.P in capillary $\rightarrow$ $\downarrow$ GFR.

e.g.: - dehydration or hypoproteinemia $\uparrow$ GFR $\downarrow$

(5) Permeability of the glomerular filtration ^{membrane} by decrease $\rightarrow$ $\uparrow$ GFR.

(6) Change in the effective filtration surface area:

e.g.: 1. Disease that destroy the glomeruli.

2. Nephrectomy

3. Sympathetic stimulation.

➤ Measurement of the GFR:

Characteristics of substance used to measure the GFR:

✓ Freely filtered.

✓ Not bound to plasma protein.

✓ Not reabsorbed or secreted by renal tubule.

✓ Not metabolized or stored in the body.

✓ Not toxic.

✓ Has no effect on filtration rate.

✓ preferably easy to measure in plasma & urine.

✓ Inulin Fructose polymer is used to measure the GFR.

- ✓ Since inulin is neither reabsorbed nor secreted.
(Amount filtered = amount secreted)

$$- GFR \times P_m = U_m \times V$$

$$- GFR = \frac{U(mg/ml) \times V(ml/min)}{P(mg/ml)}$$

$U \equiv$ Urine Concentration $V \equiv$ Urine flow rate.
 $P \equiv$ plasma Concentration.

& Procedure:

- ✓ An intravenous loading dose of inulin is given.
- ✓ Follow by sustained infusion of inulin to maintain its plasma level constant.
- ✓ Accurate timed urine sample collected (V).
- ✓ Measure the Concentration of inulin in urine (U_{in}).
- ✓ Half way through the collection urine, a blood sample is taken to measure plasma concentration of inulin (P_{in}).

$$- GFR = \frac{U_{in} \times V}{P_{in}}$$

- ✓ However inulin is exogenous.
- ✓ The subject has to be admitted to a lab or hospital to give inulin.
- ✓ Creatinine is a product of metabolism in skeletal muscle (endogenous).
- ✓ Creatinine is ^{used to} measure the GFR because:

i) It is plasma level is rather constant.

ii) It is freely filtered. $GFR = \frac{U_{Cr} \times V}{P_{Cr}}$

- ✓ A small amount of creatinine is secreted by the tubules in urine.
- ✓ Amount of creatinine excreted slightly higher than that filtered.
- ✓ However chromogenic substances in plasma give the same colour as creatinine.
- ✓ Plasma level of creatinine is slightly higher (error cancelled).
- ✓ Its advantages is that it is endogenous, therefore used clinically.

& procedure:

- ✓ Urine is collected for 24 hours.
- ✓ Amount excreted in urine is measured.
- ✓ A sample of the blood is taken to measure the plasma level of creatinine.

$$- GFR = \frac{U_{Cr} \times V}{P_{Cr}}$$

Clearance

• Clearance:

The volume of plasma from which a substance is completely cleared in one minute by excretion in the urine.

* The unit for renal plasma clearance is mL/min .

$$\text{Clearance}_x = \frac{U_x \times V}{P_x}$$

$U_x \equiv$ Concentration of (x) in urine.

$V \equiv$ Urine flow per minute.

$P_x \equiv$ Concentration of (x) in plasma.

• Clearance is used to:

- I. Measure the GFR.
- II. Measure the RBF.
- III. Assess the renal function.
- IV. Assess tubular transport mechanism of some substances or drugs.

• Inulin:

Is filtered but neither reabsorbed nor secreted

* The amount of inulin cleared in urine is that contained in the volume of plasma filtered.

- ✓ Clearance of inulin = GFR
- ✓ A substance that is filtered not reabsorbed or secreted (e.g. inulin) $\rightarrow$ Clearance = GFR
- ✓ A substance that is filtered and reabsorbed (e.g. glucose) $\rightarrow$ Clearance $<$ GFR

- ✓ A substance that is filtered & secreted (e.g. PAH) (clearance > GFR)

• Measurement of the RBF:

- RBF: Can be measured using the Fick's principle.
- BF = $\frac{\text{Amount of substance taken}}{A - V}$

• Characteristics of the substance used to measure the RBF:

- (1) Easily filtered.
 - (2) Not reabsorbed.
 - (3) Does not affect
 - (4) Not metabolized, not synthesized, Not stored by the body
- ✓ para-aminobenzoic acid (PAH) is used to measure RBF.
 - Since the kidney filters plasma

$$\text{Renal plasma flow} = \frac{\text{Amount of PAH excreted}}{RA_{\text{PAH}} - RV_{\text{PAH}}}$$

$RA_{\text{PAH}} \equiv$ Concentration of PAH in the renal artery.

$RV_{\text{PAH}} \equiv$ Concentration of PAH in the renal vein.

✓ Amount of PAH excretion = $U_{\text{PAH}} \times V$

- Since PAH is not metabolized by other tissue than:

- Arterial plasma level PAH (P_{PAH}) can be measured from plasma of any systemic artery or vein.

- PAH is highly secreted.

Venous plasma level PAH (RV_{PAH}) $\approx$ zero.

$$RPF = \frac{U_{\text{PAH}} \times V}{\text{plasma PAH}}$$

This called effective RPF, as the level of PAH in the renal venous plasma is not measured.

Effective RPF = Clearance of PAH

Tubular Function

❖ To form the Urine there are 3 main mechanisms :

1. Filtration.
2. Reabsorption.
3. Secretion.

❖ Reabsorption & Secretion, Which can be :

1. Passive
2. Active :

- ✓ primary active transport.
- ✓ Secondary active transport.

3. Hormonal dependant

* Active transport involves a carrier.

* It has a maximum upper limit for transport, due to saturation of the specific transport system.

➤ Tubular transport maximum (T_M) :

Is the maximum rate at which a substance can be actively transported.

➤ Hormonal dependant :

(i) Aldosterone : Controls reabsorption of Na^+ and secretion of K^+ & H^+ .

(ii) ADH : Controls H_2O reabsorption.

(iii) ANP : Affects Na^+ reabsorption.

(iv) Para thyroid hormone : Affects Ca^{2+} & PO_4^{2-} reabsorption.

➤ Secretion in the proximal tubule :

(i) Organic acids : Penicillin, PAH, Uric acid.

(ii) Organic bases : Histamine, Choline and creatinine.

(iii) H^+ , NH_4^+ and drugs.

Na⁺ Reabsorption

- ✓ 99.490% of filtered Na⁺ is reabsorbed in the renal tubule.
- ✓ 60-70% of filtered Na⁺ is reabsorbed in the proximal tubule.
- ✓ It is an active process.
- ✓ In the basolateral membrane Na⁺/K⁺ Pump transport Na⁺ out of the tubular cell to the interstitial space.
- ✓ Na⁺ diffuses across the luminal membranes into the tubular cell down an electrochemical gradient caused by the K⁺/Na⁺ Pump.
- ✓ Na⁺ reabsorption is the most energy consuming process in the kidney.

◆ Usually some substances are co transported with Na⁺:

1. 60-70% of the filtered H₂O is reabsorbed with Na⁺.
 || PT fluid is isotonic ||

2. Glucose by 2^{ry} active transport.

3. Amino acid also by 2^{ry} active transport.

◆ There are 5 Carriers that transport Amino acid with Na⁺ in the Luminal membrane:

① Basic

② Acidic

③ Neutral

④ proline

⑤ hydroxy proline.

* Then Amino acid will diffuse from the cell to the ECF by facilitated diffusion.

✓ PO₄²⁻, Lactate, Cl⁻ and HCO₃⁻ are also co-transported with Na⁺

Na⁺ - H⁺ antiport: Carriers carry Na⁺ into the cell and H⁺ in opposite direction.

➤ Descending limb of loop of henle:

- Highly permeable to H₂O.

- Low permeability to solutes.
- No Na^+ reabsorption.
- Thin ascending part:
 - Passive reabsorption of Na^+ & Cl^- .
- Thick ascending limb:
 - Active reabsorption of 20-25% of the filtered Na^+ , K^+ and Cl^- .
 - Na^+ is absorbed from the lumen into the cell by special carrier, which transport 1Na^+ , 1K^+ , $2\text{Cl}^- \rightarrow \text{Na}^+$, K^+ , 2Cl^- Co-transporter.
 - Then Na^+ is actively transported out of the cell by Na^+/K^+ Pump.
 - Thick ascending limb is impermeable to H_2O (Diluting Segment).

✳ Early distal tubule:

- ✓ Na^+ is reabsorbed actively by $\text{Na}^+ - \text{Cl}^-$ Co-transporter.
- ✓ Diluting segment.

◆ Late DT & CD:

Active reabsorption of 3% of the filtered Na^+ regulated by hormones:

(A) Aldosterone:

- Increase Na^+ reabsorption & K^+ secretion.

(B) ANP:

- Decreases Na^+ reabsorption.
- Na^+ is actively transported out of all segments of the renal tubule except the thin ascending limb of Henle. (passive).

تذكر! فقط في DT و CD

❖ Tubular Function ❖

Glucose reabsorption

- ✓ Normally all glucose is reabsorbed in the P.C.T.
- ✓ By 2nd active transport with Na^+ .
- ✓ In the luminal membrane, there are glucose transporters (**SGLT2**).

- * which carry Na^+ & glucose to inside the cell.
- * Na^+ is then pumped out of the cell into the interstitium by Na^+/K^+ pump.
- * Glucose is transported out of the tubular cells by facilitated diffusion aided by carriers called glucose transporters (**GLUT2**).

◆ Transport maximum (TM) for glucose:

- ✓ Is the rate by which maximum amount of glucose can be transported in one minute.
- ✓ **TM** for glucose is 375 mg/min.
- ✓ Above TM (375 mg/min) excess glucose will appear in urine.

◆ Renal threshold of glucose:

- ✓ Is the concentration of glucose in plasma that satisfies the TM for glucose and above it glucose will appear in urine (**glucosuria**).
- ✓ Renal threshold of glucose is about 180 mg/dL in the venous blood & 200 mg/dL of the arterial plasma.

◆ Osmotic Diuresis :

- ✓ The presence of large quantities of unreabsorbed solutes in renal tubules causes an increase in

Urine volume.

- ✓ Solutes that are not reabsorbed in the PCT causes Osmotic effect. = "They hold water in the tubules"
- e.g: polyurea in diabetes mellitus, Mannitol.

K⁺ Reabsorption & Secretion

➤ In the p.c.t.:

- 60-70% of the filtered K⁺ is reabsorbed by both active & passive mechanism.

➤ In the loop of henle:

- 20-25% of the filtered K⁺ is absorbed by Na⁺, K⁺, 2Cl⁻ transporters.
- By the time the filtrate reach the distal part most of K⁺ is already reabsorbed.

➤ In the DT & CD:

- K⁺ secretion & Na⁺ reabsorption by the principle cells through epithelial Na channel (ENaC).

- K⁺ secretion is regulated by:

(i) Aldosterone hormone.

(ii) plasma level of K⁺.

* hyperkalemia directly stimulates aldosterone.

(iii) Flow rate of tubular fluid.

* ↑ Flow → ↑ K⁺ secretion.

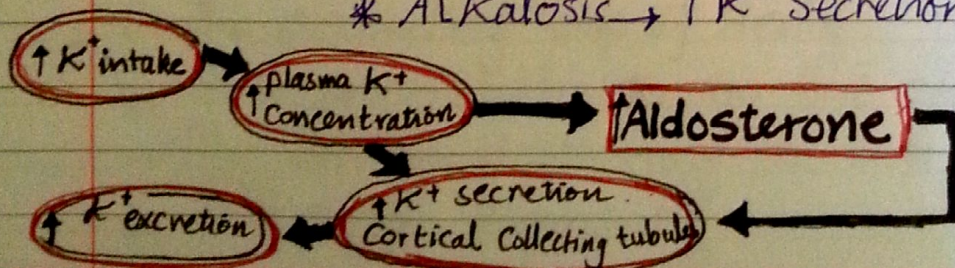
(vi) Na⁺ concentration in the tubular fluid.

* ↑ Na⁺ → ↑ K⁺ secretion.

(v) H⁺ Concentration.

* Acidosis → ↓ K⁺ secretion → hyperkalemia.

* Alkalosis → ↑ K⁺ secretion → hypokalemia.



Water reabsorption

- ✓ 180 L of fluid is filtered per day.
- ✓ 99.4% of the filtered water is reabsorbed.
- ✓ Urine volume is 1-1.5 L/day.

❖ Obligatory urine volume:

- Is the minimum volume of urine to be passed out to maintain normal renal function.
 - **500 ml/day**.
 - The maximum amount of urine in the absence of ADH is 23 L/day.
 - water reabsorption is passive process in all renal tubular segments.
- It follows the osmotic gradient.

➤ In the P.C.T :

- **60-70 %** of H_2O is reabsorbed.
 - passively following the osmotic gradient created by Na^+ reabsorption.
 - There are aquaporin-1 channels facilitating H_2O reabsorption.
 - In the P.C.T the tubular fluid is isotonic.
- Osmolarity of the Cortex is **300 mosm/L** (similar to plasma).
- In the medulla osmolarity increases gradually as we move deeper, until it reaches a maximum of **1200 mosm/L** at the tip of the medulla.

➤ In the descending loop of Henle :

- **15-20 %** of the filtered H_2O is reabsorbed passively.
- Following the high osmotic gradient of the medullary tissue.

➤ In the ascending loop of Henle :

- It is impermeable to H_2O but solutes are reabsorbed.
- Tubular fluid leaving the loop is hypotonic.
- Diluting segment.

❖ Late DT & CD :

- H_2O reabsorption is controlled by ADH.
- ADH increases the permeability of the collecting ducts to H_2O .
- In the late & CD : ADH bind to V_2 receptors → Insert aquaporin-2 Channels → in the luminal membrane → increase permeability to H_2O .
- 10% of the filtered H_2O is reabsorbed in the cortical CD
(tubular fluid isotonic)
- In the medullary CD : 4.5% or more of the filtrate is reabsorbed into the hypertonic medullary interstitium.
- In the human urine osmolality reach 1400 mosm/Kg H_2O .
- 99.7% of the filtered H_2O is reabsorbed.

❖ Factors that Stimulate ADH secretion :

- ✓ Increase Osmolality of the ECF.
- ✓ Decrease ECF volume.
- ✓ Pain & Stress.

⊗ When ADH is absent :

- CD epithelium is relatively impermeable to H_2O .
- Large amount of hypotonic tubular fluid → renal pelvis
(13% of the filtered H_2O).
- Impermeability of CD is not absolute.
- 2% of the filtered H_2O is reabsorbed along with solutes in the absence of the ADH.

◆ In the absence of ADH → (Diabetes insipidus).

- Urine volume is 23 L/day.
- Urine flow $\geq$ 15 ml/min.
- Osmolality of urine is 30 mosm/Kg H_2O .

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Concentration of Urine

Concentrated or dilute urine is formed by regulate the plasma osmolarity by changing the amount of water excreted in urine.

❖ Formation of concentrated urine :-

⊗ Factors needed to form concentrated urine :-

- ✓ Hypertonic medulla.
- ✓ Maintain the medulla hypertonic.
- ✓ High ADH.

➤ Hypertonic medulla :

Gradient osmolarity from 300 mosm/L in the cortex to 1200 mosm/L in the medulla & it is **formed by:**

1. **Active reabsorption:** of NaCl in the thick ascending part of the loop of Henle (most important).
2. **Passive reabsorption:** of NaCl in the thin ascending part of the loop of Henle.
3. **Urea recycling:** the ascending limb of Henle and the terminal part of CD in the medulla are permeable to urea.
 - ✓ ADH → ↑ reabsorption of urea in the deepest part of CD
 - ✓ Urea diffuse out of the deepest part of CD → The ascending limb of the Henle.
 - ✓ Urea recycling (trapped): Interstitial Fluid → hypertonic medulla.
4. **Counter current multiplier system :**
 - ✓ It is a system in which the inflow is parallel to the outflow.

- ✓ opposite direction.
- ✓ In close proximity to the outflow
- ✓ The outflow influence the inflow.

➤ To maintain the medullary hypertonic:

• Counter current exchanger system:

- Vasa recta are U-shaped long vessels that parallel loops of Henle of the juxtamedullary nephrons.
- the vasa recta are freely permeable to H_2O , NaCl and urea.

• Descending part:

- at any level blood has lower osmolarity than the medulla.

($H_2O \rightarrow$ out, Solute $\rightarrow$ in).

• Ascending part:

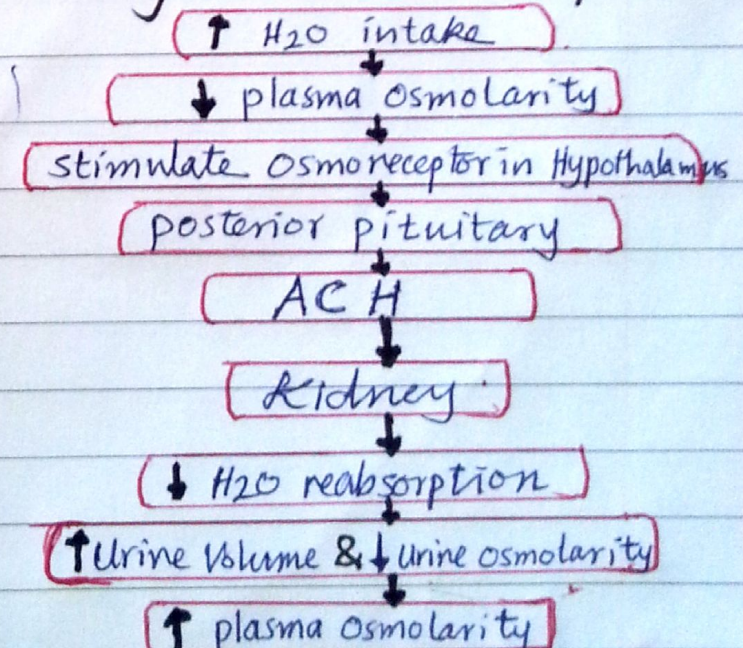
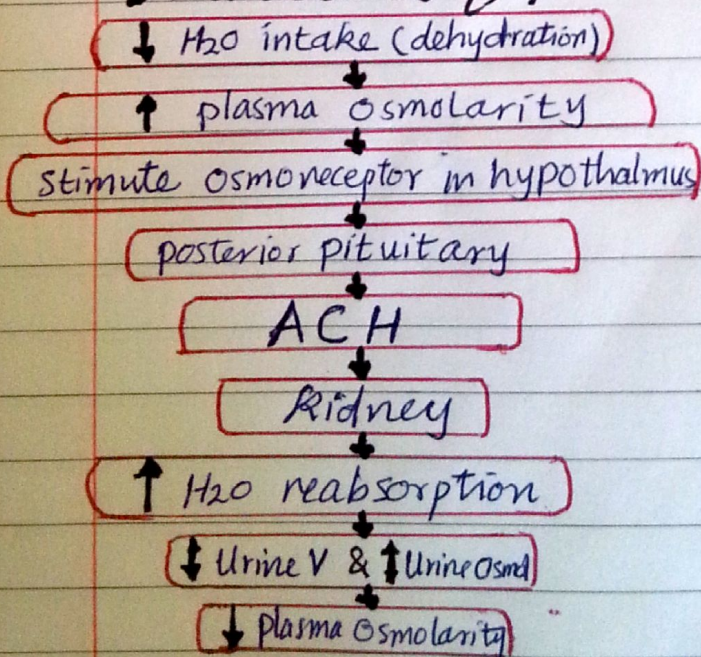
- at any level blood has higher osmolarity than the medulla.

(Solute $\rightarrow$ out, $H_2O \rightarrow$ in).

- H_2O passes into vessel, NaCl and urea trap within the interstitial fluid.

- Low blood flow in the medulla help to maintain the medulla hypertonic.

➤ Homeostasis of plasma Osmolarity is maintained by ADH:



♦ Counter current mechanism:

✓ Active reabsorption of NaCl in the ascending part $\rightarrow$ $\uparrow$ Osmolarity of the interstitium $\rightarrow$ H_2O moves from the descending part till equilibrate with interstitium.

✓ Salt reabsorption in ascending limb $\rightarrow$ $\uparrow$ the concentration fluid entering the descending limb multiplies the concentration of the interstitial fluid and the descending limb fluid $\rightarrow$ hyper tonic medulla.

تجزئة الماء وتوزيعه

Renin Angiotensin System

- ✓ Renin secreted from juxta glomerular apparatus (JGA).
- ✓ the JGA is a part of the nephron where the afferent arteriole comes into contact with the last part of thick ascending limb of the loop.
- ✓ Granular cells within the afferent arteriole secrete renin in the blood. (JG Cells).
- ✓ The part of the ascending limb of the loop in contact with the granular cells of the afferent arteriole is called the macula densa.
- ✓ The JGA is formed of:
 - (a) The macula densa.
 - (b) The JG cells.
 - (c) The Lacis cells.

❖ Factors which stimulate the JGA to secrete renin are:

- i. Renal ischemia.
- ii. Hyponatremia.
- iii. Sympathetic.

❖ Effect of angiotensin II:

1. Vaso constriction.
2. Stimulates ADH secretion.
3. Stimulates aldosterone.
4. Stimulates Thirst Centre.
5. Stimulates sympathetic.
6. Contraction of mesangial cells $\downarrow$ GFR.
7. $\uparrow$ Na^+ reabsorption.
8. $\uparrow$ ACTH secretion.

* Renin Angiotensin blockers are used for treatment of hypertension : e.g.:-

1. Captopril (ACE inhibitor)
2. Enalapir (ACE inhibitor)
3. Losartan (Blocks AT_1)

Micturition

- Micturition is a spinal reflex.
- Facilitated and inhibited by higher brain centers.
- There is a facilitatory area in the pons and inhibitor area in the midbrain.
- The ureters contain smooth muscles regular peristaltic contractions occurring is 1-5 times/min.
- This move the urine from the renal pelvis to the bladder.
- Normally, The ureters enter obliquely through the bladder wall.
- This prevent reflux of urine from the bladder into ureters.
- Changes in intravesicular pressure as the bladder fills with urine can be described by cystometrogram.

❖ Cystometrogram :

- ✓ Empty bladder the intravesicular pressure is about zero.
- ✓ 30-50 ml of urine, the pressure rises to 5-10 cm H_2O .
- ✓ 200-300 ml, Cause only a small rise in pressure.
- ✓ Bladder muscle has the property of plasticity.
- ✓ 300-400 ml of urine in the bladder, the pressure rises rapidly.
- ✓ The first urge to void is felt at bladder volume of about 150 ml.
- ✓ A marked sense of fullness at about 400 ml.
- ✓ Internal sphincter of the urethra is supplied by parasympathetic.

- ✓ External sphincter of the urethra is supplied by Somatic Nerve.

❖ Micturition reflex:

- I. **Stretch receptors:** In the wall of the bladder stimulated by stretch.
- II. **Afferent:** Parasympathetic.
- III. **Center:** Sacral segment of spinal cord (S_2, S_3, S_4).
- IV. **Efferent:** Parasympathetic.
- V. **Response:**
 - ✓ Contractions of the detrusor muscle of the urinary bladder.
 - ✓ Relaxation of the internal sphincter.
 - ✓ if the condition is suitable external sphincter relax and urine pass out.
 - ✓ if the condition is not suitable external sphincter remain contracted.
 - ✓ Reflex fade away & come again later.

❖ Abnormalities of micturition:

- When the afferent nerves are at all reflex contractions of the bladder are abolished.
- The bladder becomes distended, thin walled & hypotonic. But there are some contractions because of the intrinsic response of smooth muscle to stretch.
- When the afferent & efferent nerves are both destroyed (**tumors**) the bladder is flaccid and distended.
- Then many contraction waves occur → dribbles of urine out of the urethra.
- The bladder becomes shrunken and hypertrophied.

❖ Effects of spinal cord transection:

- During spinal shock, The bladder becomes Overfilled and urine dribbles out (over flow in continence).
- After spinal shock has passed the voiding reflex returns, But no voluntary control.
- Some paraplegic patients train themselves to Initiate voiding by pinching or stroking their thighs (mass reflex).

تم بحمد الله وتوفيقه

في ليلة الاثنين ١٢/١٢/١٤٣٦ هـ
ووافق ٦/١٢/ديسمبر ٢٠١٤ م

نسألكم الدعاء...

وجزاكم الله خيرا...